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EXAMINER
HUI, SAN MING R

ART UNIT	PAPER NUMBER
1617	6

DATE MAILED: 03/12/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/509,677	II ET AL.	
	Examiner	Art Unit	
	San-ming Hui	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

P riod for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 December 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-25* is/are pending in the application.

4a) Of the above claim(s) *21-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The cancellation of claim 2 in the amendment filed December 6, 2001 is acknowledged. The addition of claims 21-25 in the amendment filed December 6, 2001 is acknowledged.

Claims 1 and 3-25 are pending.

The outstanding rejection of claims 19 and 20 under 35 USC 112, second paragraph regarding the term "taking ability" is withdrawn in view of the amendments to the claims filed December 6, 2001.

Newly submitted claims 21-25 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: the method of masking the taste comprising a different method steps and different modes of operation. The originally filed claims 19 and 20, the only claims drawn to a method of masking taste of an oral preparation, operates by administering a composition consisting essentially of a drug, a sugar alcohol, and a pH adjusting agent. Method of claim 21 operates by the employment of pH adjusting agent to increase the pH in the oral cavity to the pKa value or more of the drug. It also involves the steps causing the un-dissociation of the basic group and the reduction of solubility of the drug in the oral cavity. Method of claim 22, however, operates by the employment of a drug compound and changing the taste of the drug by increasing its solubility in fat. Method of claim 23 operates by the employment of an amphoteric drug and forming an intermolecular salt or a salt of the pH adjusting agent, without the employment of sugar alcohol. Method of claim 25 operates by the employment of an amphoteric drug compounds and

eliminating the acid addition salt and converting the drug into free form using pH adjusting agent.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 21-25 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 3-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for drug compounds listed in specification from page 6, line 15 to page 8, line 5, does not reasonably provide enablement for any other drug with unpleasant tastes. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required

undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,

2) the amount of direction or guidance provided,

3) the presence of absence of working examples,

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art

7) the predictability of the art, and

8) the breadth of the claims.

Applicant fails to set forth the criteria that defines a drug with "unpleasant taste". Additionally, Applicant fails to provide information allowing the skilled artisan to ascertain these compounds without undue experimentation. There is no adequate direction provided by the applicant as to how to select other drugs with unpleasant tastes which would be suitable in the instant invention. Additionally, Applicant fails to provide information allowing the skilled artisan to ascertain these compounds without undue experimentation. Applicant has not provided sufficient biochemical information (e.g. molecular weight, melting point, refractive index, etc.) that distinctly identifies compounds other than those encompassed by compounds having unpleasant taste. While a "drug with unpleasant taste" may have some notion of the activity of the "drug"; claiming biochemical molecules by function only fails to enable the skilled artisan to

make and use the scope of such molecules, as there is insufficient guidance and direction as to structure of the "drug", broadly encompassed by the claimed invention.

Furthermore, the instant specification does not provide any working examples to point out how other drugs with unpleasant tastes other than the compounds listed in the specification from page 6, line 15 to page 8, line 5 may be used successfully in the claimed invention. In other words, only a limited number of drugs with "unpleasant taste" examples are set forth, thereby failing to provide sufficient working examples. It is noted that these examples are neither exhaustive, nor define the class of compounds required. The pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity.

Moreover, it is well known in the art that structural differences in active compounds will impart different chemical, physical, and therapeutic properties to the same compounds. Therefore different drug compounds with unpleasant tastes, other than the ones listed in specification from page 6, line 15 to page 8, line 5, may be reasonably expected to yield a different result. The instant claims read on all drugs with "unpleasant taste", necessitating an exhaustive search for the embodiments suitable to practice the claimed invention. Applicants fail to provide information sufficient to practice the claimed invention, absent undue experimentation.

Response to Remarks regarding rejection under 35 USC 112, first paragraph

Applicant's remarks filed December 6, 2001 regarding enough guidance are being provided in the specification page 5, lines 5-14 have been considered but are not

found persuasive because the specification page 5, lines 5-14 disclosing "the compound having unpleasant taste, especially a bitter taste, include a compound which at least one basic group in its structure, ... a solvate of an acid addition salt of the compound and the like. In this case, the basic group means a primary amino group ... a quaternary amino group or the like group, and its illustrative examples include amino group ,... and the like.". The compounds with unpleasant taste are including various classes of compounds herein. Therefore, one of skill in the art could ascertain which specific compounds from the disclosed classes of compounds would be useful in the claimed invention without undue experimentation.

Applicant asserts that the examiner solely rely on an alleged "unpredictability" in the art of structural differences in the compounds in the rejection under 35 USC 112, first paragraph have been considered but not found persuasive because of the reasons set forth above in the rejection under 35 USC 112, first paragraph.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 3-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The expression "unpleasant taste" in claim 1, 9, and 19 is a relative term which renders the claim indefinite. The expression "unpleasant taste" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite

degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Applicant's remarks regarding the specification page 5, lines 5-14 lists examples of drugs having unpleasant taste have been considered but are not found persuasive because even though the specification page 5, lines 5-14 lists some examples of drugs having unpleasant taste, it is still unclear what drugs are encompassed by the claims because these examples are neither exhaustive, nor define the class of compounds required. It is unclear what agents other than example compounds disclosed are encompassed by this term.

The expression "bitter taste" in claim 2 is a relative term which renders the claim indefinite. The expression "bitter taste" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is unclear as to what drugs are encompassed by the claims. Applicant's remarks regarding definition of "bitter taste" is disclosed in the specification have been considered but are not found persuasive because some compounds are bitter to some but not to others. It is unclear what agents other than example compounds disclosed are encompassed by this term.

The term "corrective agent" in claims 16 and 20 renders the claims indefinite as to the agents are encompassed by the claims. This term is not understood. It is unclear what the corrective agents herein are intend to correct. Applicant's remarks regarding examples of "corrective agents" are disclosed in the specification have been considered but are not found persuasive because there is no single common function or properties

among the corrective agents listed in page 15 in the specification. It is noted that these examples are neither exhaustive, nor define the class of compounds required. It is unclear what agents other than example compounds disclosed are encompassed by this term.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3-7, 9, 12-14, 16-18 are rejected under 35 U.S.C. 102(b) as being anticipated by Pearmain (US Patent 5,188,839).

Pearmain teaches cimetidine tablet, which improve palatability, that consists essentially of a pH adjusting agents: sodium bicarbonate, a sugar alcohol: sorbitol and a sweetener: aspartame (See particularly the abstract, col.4, example 3). Pearmain also teaches the ratio between sorbitol and cimetidine is about 3.5 to 1; the ratio between sodium bicarbonate and cimetidine is about 0.9 to 1 (See particularly col. 4, example 3).

Response to Remarks regarding rejection under 35 USC 102

Applicant's remarks regarding Pearmain not teaching the claimed sugar alcohol properties have been considered but are not found persuasive because Products of identical chemical composition can not have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are

necessarily present. *In re Spada* 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01. In the instant case, the prior art teaches the same sugar alcohol herein.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 8, 10-11, 15, 19, and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pearmain (US Patent 5,188,839) in view of Hoshino (WO 97/12606, English equivalent, US Patent 6,146,661, is also provided).

Pearmain teaches cimetidine tablet, which improve palatability, that consists essentially of a pH adjusting agents: sodium bicarbonate, a sugar alcohol: sorbitol and a sweetener: aspartame (See particularly the abstract, col.4, example 3). Pearmain also teaches the ratio between sorbitol and cimetidine is about 3.5 to 1; the ratio between sodium bicarbonate and cimetidine is about 0.9 to 1 (See particularly col. 4, example 3).

Pearmain does not expressly teach that erythritol, the sugar alcohol, is in the cimetidine tablet. Pearmain does not expressly teach that the ratio between the sugar alcohol to cimetidine is from 5 to 10 : 1. Pearmain does not expressly teach that the pH values of the solution of the pH adjusting agent be equal to or higher than that of the solution of cimetidine. Pearmain does not expressly teach a method of masking the taste of an oral preparation employing the cimetidine tablet with improved palatability.

Hoshino teaches a chewable tablet that is free from unpleasant intrabuccal (oral) sensation which may contain a H_2 receptor blocking agent including cimetidine and erythritol (See abstract, claim 1). Hoshino also teaches a method of improving the unpleasant taste of the tablet with sugar alcohol herein, including erythritol (See col. 1, lines 51-58; col. 2, lines 25-56 particularly, and col. 6, line 1 to 60).

It would have been obvious for one of ordinary skill in the art at the time the invention was made to employ the sugar alcohol, erythritol in the cimetidine tablet of Pearmain, with the ratio between the sugar alcohol to cimetidine being from 5 to 10 : 1 and the pH values of the solution of the pH adjusting agent be equal to or higher than that of the solution of cimetidine.

It would have been obvious for one of ordinary skill in the art at the time the invention was made to employ the cimetidine tablet in a method of improving "taking ability".

One of ordinary skill in the art would have been motivated to incorporate erythritol into the cimetidine tablet of Pearmain because it is known in the art that erythritol is useful to improve from unpleasant intrabuccal (oral) sensation in chewable tablet compositions. The incorporation of erythritol to improve the taste of a cimetidine tablet is therefore *prima facie* obvious.

Optimization of result effect parameters (i.e., ingredient amounts, solutions, or suspension, pH values) is obvious as being within the skill of the artisan, absent evidence to the contrary.

One of ordinary skill in the art would have been motivated to employ the cimetidine tablet of Pearmain as modified by Hoshino in a method of improving taking ability because the tablet would be expected to have improved taste and oral sensation and therefore the tablet would have been reasonably expected to be more pleasant to "take" or ingest orally.

It is applicant's burden to demonstrate unexpected results over the prior art. See MPEP 716.02, also 716.02 (a) - (g). Furthermore, the unexpected results should be demonstrated with evidence that the differences in results are in fact unexpected and unobvious and of both statistical and practical significance. *Ex parte Gelles*, 22 USPQ2d 1318, 1319 (Bd. Pat. App. & Inter. 1992). Moreover, evidence as to any unexpected benefits must be "clear and convincing" *In re Lohr*, 137 USPQ 548 (CCPA 1963), and be of a scope reasonably commensurate with the scope of the subject matter claimed, *In re Linder*, 173 USPQ 356 (CCPA 1972). In the instant case, the data from examples 1-4 in pages 20-26 in the specification have been considered but are not found persuasive because the data in example 1 merely demonstrates no bitterness was observed in the taste masking composition without the active drug. This is seen to be the expected results over the cited prior art. The example 2 demonstrates that the addition of a sweetener, aspartame would improve the bitter taste of the cimetidine containing composition. This is also considered as expected result in view of the cited prior art. Example 3 examines different sugar alcohols used in the taste masking composition. The data in example 3 demonstrates only certain sugar alcohols such as xylitol, D-mannitol, D-Sorbitol and maltitol are useful in the taste masking composition.

This is seen to be an expected effect based on the cited prior art. Example 4 evaluates the taste masking composition with different active drug compounds. It demonstrates that the taste masking composition is effective in masking the bitter taste of different active drugs. This is seen to be an expected effect based on the cited prior art. No convincing and clear unexpected result is seen.

Response to Arguments regarding rejection under 35 USC 103

Applicant's arguments filed December 6, 2001 regarding Pearmain not teaching or suggesting the claimed invention have been fully considered but they are not persuasive. This is because this is a rejection under 35 USC 103, which is not an anticipation rejection.

Applicant's remarks filed December 6, 2001 regarding Hoshino teaching a method of improving intrabuccal sensations (e.g., discomfort such as roughness or dustiness in the mouth) and therefore no motivation or suggestion being provided to combine the teaching of cited prior arts to arrive at the claimed invention have been considered. The remarks are not found persuasive because Hoshino teaches that intrabuccal sensation includes, but not limit to, discomfort such as roughness or dustiness in the mouth. Furthermore, Hoshino teaches the employment of sugar alcohol to improve the intrabuccal sensation of a cimetidine oral dosage form. Sugar alcohol is commonly known to be sweet (See Hoshino col. 2, line 65). Therefore, employing sugar alcohol herein would have been reasonably expected to improve the roughness or dustiness and taste of the same. The combined teaching of Pearmain

and Hoshino clearly renders the claims herein obvious because employing the ingredients herein (i.e., sugar alcohol, pH adjusting agent, and sweetener) would have been reasonably expected to be useful in formulating a better palatable oral administration preparation.

Applicant's remarks filed December 6, 2001 regarding the instant invention being drawn to a oral taste masking composition which are dissolved completely or partially in the oral cavity before swallowing the same have been considered but are not found persuasive because both Pearmain and Hoshino teach the compositions can be formulated into chewable tablets.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (703) 305-1002. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Minna Moezie, J.D., can be reached on (703) 308-4612. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

San-ming Hui
February 28, 2002

MINNA MOEZIE, J.D.
SUPERVISORY PATENT EXAMINER
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